GLOBAL BIOTECHNOLOGY RISK ASSESSMENT MASTER INDEX

BIOLOGICS | MONOCLONAL ANTIBODIES | VACCINES | RECOMBINANT | CELL & GENE THERAPIES

API / DRUG SUBSTANCE • INTERMEDIATES • STERILE / NON-STERILE BIOPROCESSING • QC & ADL

ICH Q9(R1) / Q5A(R2) | EU GMP Annexes 1 & 2 / ATMP Part IV | US FDA | WHO | MHRA | TGA | CDSCO / Schedule M

Document code	ISHA-BT-RA-MASTER-001
Revision / issue date	Rev 00 | 05 November 2026
Equipment, process and system topics	886 distinct topics
Proposed micro-level risk scenarios	2,658 in companion scored Excel register
Functional areas / departments	41
Register status	Proposed screening inventory - site applicability and approval required

Prepared by: ISHA'S GMP CONSULTANCY PRIVATE LIMITED

India: +91 86675 89984 | +91 99764 91578 | info@ishasgmp.com | project@ishasgmp.com | www.ishasgmp.com

EXECUTIVE PURPOSE & APPLICABILITY

This master index identifies potential risk assessment subjects across biotechnology R&D, manufacturing and GMP operations: microbial and mammalian culture, cell banks, media, fermentation, upstream and downstream purification, virus safety, drug substance and intermediates, recombinant proteins, monoclonal antibodies, vaccine antigens, mRNA/LNP, viral vectors, plasmid/genome editing, autologous/allogeneic cell therapy, plasma-derived products, ADCs, sterile filling, lyophilization, laboratories, utilities, and corporate/support processes.

The accompanying Excel workbook contains three proposed micro-level failure scenarios for each topic, with distinct failure pathways, potential effect, suggested controls and evidence fields. These are analytical prompts; none is a finding at any real manufacturing site. Each user must define actual hazards, existing validated controls, objective evidence, scoring, acceptance, residual risk, action ownership and independent approvals.

CORE ASSESSMENT METHOD & LIMITATIONS

1. Establish product/platform, patient risk, intended clinical use and applicable markets before assessing equipment/activities.

2. Map critical quality attributes (identity, purity, potency, safety, stability) to process control points and failure mechanisms; select PHA, process FMEA, HAZOP, HACCP, contamination risk, virus risk, fault tree or statistical analysis accordingly.

3. The Excel S × O × D score is only an optional prioritization aid. Numerical RPN can mask catastrophic hazards and must not substitute for risk acceptance, sterility/viral-safety assurance or clinical benefit-risk judgment.

4. For CGT and gene therapy, separately document donor/recipient identification, chain of identity/custody, genomic/genotoxic risk, viral replication competence, cell viability/potency and product traceability.

5. Maintain occupational/biosafety/EHS risk reviews under applicable laws and agent-specific engineering containment controls, separately from patient/product GMP quality risk.

6. All risk controls must have demonstrable effectiveness, owner, approval, review triggers, controlled records and scientifically justified residual risk decisions.

REGULATORY ALIGNMENT & IMPORTANT DISTINCTIONS

Core references include ICH Q9(R1), Q10, Q5A(R2), Q5E and Q6B, WHO GMP for biological products (TRS 999 Annex 2), EU GMP Annex 2 for conventional biological medicinal substances/products and Annex 1 for sterile manufacturing, and EU GMP Part IV for advanced therapy medicinal products (ATMPs). Select additional FDA, MHRA, TGA and CDSCO rules based on product and market. For US products, 21 CFR Parts 210/211 and 600 series may be relevant, while 21 CFR Part 1271 only applies where the HCT/P legal classification is met.

India regulatory note: Revised Schedule M (not Schedule Y) governs applicable pharmaceutical GMP requirements. For clinical-trial and new-drug permissions, assess New Drugs and Clinical Trials Rules 2019 and amendments. Historic Schedule Y is not used as the main current clinical-trial compliance anchor. Special biosafety/GMO, blood/plasma and cell-therapy rules depend on activity.

MASTER FUNCTIONAL COVERAGE

Function / department	Topics	Risk scenarios
ADL / Characterization / Method Lifecycle	25	75
Adventitious Agent & Viral Clearance	22	66
Aseptic Processing & Personnel	24	72
Autologous / Allogeneic Cell Therapies	25	75
Cell Bank, Seed Lot & Genetic Stability	22	66
Chromatography & Resin Systems	28	84
Cleanroom / HVAC / Facility Containment	21	63
Clinical Safety / Pharmacovigilance	17	51
Conjugates, ADCs & High-Potency Biologics	12	36
Drug Substance Formulation & Bulk Holding	20	60
EHS / Biosafety / Environmental	25	75
Engineering / Equipment Maintenance	25	75
HR / Admin / Personnel Competency	15	45
IT / CSV / Automation / Data Integrity	25	75
Inoculum Preparation / Seed Train	20	60
Labelling / Pack / Serialization	18	54
Lyophilization / Freeze Drying	24	72
Microbial Fermentation	24	72
Microbiology / Sterility / Adventitious QC	21	63
Plasma-Derived Biologicals	16	48
Plasmid DNA / Gene Editing	20	60
Primary Harvest / Clarification	20	60
Purchase / Supplier / Outsourcing	20	60
QA / Quality Management System	20	60
QC Analytical / Bioassay Laboratory	34	102
Quality Assurance / Risk Governance	16	48
R&D / Cell Substrate Development	20	60
Raw Materials, Media and Buffers	22	66
Regulatory Affairs / CMC	20	60
Single-Use Systems / Bioprocess Assemblies	20	60
Stability / Cold Storage & CCIT	20	60
Technology Transfer / Scale-up / CPV	20	60
UF/DF, Filtration & Concentration	22	66
Upstream Mammalian Cell Culture	26	78
Vaccine / Antigen Manufacturing	20	60
Validation, Qualification & PPQ	28	84
Vial, Syringe & Cartridge Filling	23	69
Viral Vector and Gene Therapy	25	75
Warehouse / Materials / Cold Chain	20	60
Water, Steam, Gases & Utilities	21	63
mRNA / LNP Platforms	20	60

REGULATORY REFERENCE KEY

Code	Regulatory / guidance reference	Intended scope / applicability note
Q9	ICH Q9(R1): Quality Risk Management	Formal lifecycle quality risk management; risk acceptance scientific and site-specific
Q10	ICH Q10: Pharmaceutical Quality System	PQS, lifecycle process performance, change and continual improvement
ICHQ5	ICH Q5B/C/D family: biotechnology quality	Expression constructs, stability and cell substrate / cell bank principles, as applicable
Q5A	ICH Q5A(R2): Viral Safety Evaluation	Cell lines of human or animal origin and risk-based virus testing / clearance
Q5E	ICH Q5E: Comparability of biotechnological/biological products	Manufacturing process changes and quality attribute comparability
Q6B	ICH Q6B: Specifications - biotechnology/biological products	Specification, analytical procedures and acceptance criteria
EU1	EU GMP Annex 1: Manufacture of Sterile Medicinal Products	Sterile bioprocessing, contamination control and aseptic processing where applicable

Code	Regulatory / guidance reference	Intended scope / applicability note
EU2	EU GMP Annex 2: Manufacture of Biological Active Substances and Products	Biologic manufacturing including biological starting materials; not replacement for ATMP Part IV
ATMP	EU GMP Part IV: Advanced Therapy Medicinal Products	EU specific GMP for ATMPs; distinct from Annex 2 conventional biologics
WHO999	WHO TRS 999 Annex 2: GMP for Biological Products	Vaccines, biotherapeutics and biological GMP principles
FDA600	US FDA 21 CFR Parts 600-680 and 210/211 as applicable	Biological products and cGMP controls; classification/product-specific US requirements
FDA1271	US FDA 21 CFR Part 1271 as applicable	Human cells/tissues or HCT/P product category; legal classification required
SCHM	India revised Schedule M (2023, as amended)	GMP and premises, plant/equipment for pharmaceutical products in India
INDNDCT	India New Drugs and Clinical Trials Rules, 2019	Clinical trials/new drug framework, subject to product and activity applicability
TGA	Australian TGA medicinal products GMP and biologics	Australia manufacturing/licensing/sponsor and standard applicability
MHRA	UK MHRA GMP/biological medicinal products	UK GMP and relevant guidance for products/manufacturing
CFR11	US 21 CFR Part 11: Electronic Records / Signatures	GxP electronic records, relevant when used to satisfy FDA record requirements
ANN11	EU GMP Annex 11: Computerised Systems	GMP computerised system validation, audit trails and data governance
Q7	ICH Q7: GMP Guide for APIs	API processes, intermediates and relevant lifecycle elements; suitability to specific biologics
EHS	Applicable biosafety / GMO / worker and environment legislation	National and site-specific biosafety, environmental, occupational permits

Official URLs for all references are available in the REGULATORY SOURCES worksheet of the Excel workbook.

01 | ADL / CHARACTERIZATION / METHOD LIFECYCLE

25 distinct assessment topics • 75 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
ADL-001	Analytical target profile definition	method intended use and performance	method not fit for release decision
ADL-002	Assay specificity and matrix effects	coeluting species and interference	wrong CQA measurement
ADL-003	Assay accuracy and recovery	bias over product range	potency or purity misestimated
ADL-004	Assay precision intermediate	analysts, labs, days and instruments	false batch variability decisions
ADL-005	Assay linearity and range	calibration relationship and concentration	poor quantitation at limits
ADL-006	Assay detection/quantitation limits	sensitivity relative to specification	low-level impurity missed
ADL-007	Assay robustness DoE	critical method parameters	transfer or equipment causes failures
ADL-008	Stability-indicating method design	degradation/forced degradation	unstable batch incorrectly accepted
ADL-009	Method comparability after equipment change	detector/column software versions	method shift mistaken for product drift
ADL-010	Assay validation protocol control	predefined tests, criteria and deviations	post-hoc acceptance of invalid method
ADL-011	QC method transfer protocol	receiving lab equivalence and training	site-to-site inconsistent lot disposition
ADL-012	Potency reference standard bridging	unit assignment and new standard	potency drift across reference lots
ADL-013	Structural elucidation by orthogonal methods	native structure and functional activity	undetected structural alteration
ADL-014	Protein oxidation site mapping	methionine and tryptophan changes	reduced biological activity not linked
ADL-015	Deamidation and isomerization assessment	site-specific degradation	changed potency or immunogenicity
ADL-016	Disulfide bond mapping	correct linkages and scrambling	misfolded protein accepted
ADL-017	HCD/NGS sequence integrity	sequence variants and analysis pipeline	unexpected sequence variant undetected
ADL-018	Glycosylation site occupancy assessment	glycan profile and site occupancy	altered bioactivity/clearance
ADL-019	Subvisible particle methods MFI/HIAC	proteinaceous particle discrimination	inadequate particulates risk evaluation
ADL-020	DSC/DSF thermal stability	transition temperature and repeats	misleading formulation selection
ADL-021	Circular dichroism secondary structure	instrument baseline and matrix	structural change missed
ADL-022	NMR/Higher order structure methods	spectral controls and comparability	subtle folding difference not identified
ADL-023	ELISA/ligand-binding bridging	lot-to-lot reagent qualification	false potency comparability results
ADL-024	Biological assay statistical parallelism	dose response and validity	biased relative potency value
ADL-025	Assay lifecycle continued verification	control chart and drift signals	long-term assay performance deterioration

02 | ADVENTITIOUS AGENT & VIRAL CLEARANCE

22 distinct assessment topics • 66 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
VIR-001	Cell substrate viral agent testing	risk-based animal/human virus panel	unknown adventitious virus in culture
VIR-002	Raw material viral risk evaluation	serum/hydrolysate and geographic sourcing	infectious input to production
VIR-003	Retrovirus assessment in cell lines	endogenous and exogenous retroviral agents	viral contamination risk
VIR-004	In-process adventitious agent testing	sampling stages and assay detection limits	contaminated harvest unnoticed
VIR-005	Virus spike-study model selection	relevance of enveloped and nonenveloped viruses	overstated clearance assurance
VIR-006	Virus clearance study scale-down	representativeness, load and residence time	invalid log-reduction claims
VIR-007	Low-pH viral inactivation	pH, time, temperature and mixing	insufficient viral inactivation
VIR-008	Viral inactivation tank pH mapping	minimum/maximum pH and time	local untreated hold pockets
VIR-009	Viral inactivation neutralization	correct end pH and rate	protein aggregation or residual low pH
VIR-010	Solvent-detergent viral inactivation	reagent concentration and contact time	incomplete enveloped virus inactivation
VIR-011	Solvent detergent residual removal	residual controls and downstream effects	toxic reagent in final bulk
VIR-012	Nanofiltration virus filter integrity	pore integrity and system seal	virus breakthrough
VIR-013	Virus filtration load and pressure	fouling and flux limits	loss of virus retention assurance
VIR-014	Virus removal in chromatography	resin state, load and matrix applicability	clearance not transferable
VIR-015	Orthogonal viral clearance strategy	independent complementary steps	common-mode breakthrough of infectious agent
VIR-016	Virus assay interference	product cytotoxicity and assay suitability	false negative viral test
VIR-017	Virus assay reference standards	titer, potency and controls	incorrect clearance calculation
VIR-018	Virus clearance lifetime study	resin/filter use and aged condition	end-of-life viral clearance inadequate
VIR-019	Bacterial/viral segregated processing	pressure and dedicated handling	virus seed contaminates sterile biologics
VIR-020	Unexpected viral signal investigation	quarantine and batch genealogy	infected material used downstream
VIR-021	Viral risk review after raw material change	novel animal-derived component and supplier	viral safety claim no longer justified
VIR-022	Viral clearance process change comparability	new pH/flow/hold parameter	clearance claim invalidated

03 | ASEPTIC PROCESSING & PERSONNEL

24 distinct assessment topics • 72 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
ASEP-001	Contamination control strategy (CCS)	facility/process integrated microbial risk	uncontrolled sterility hazard
ASEP-002	Grade A critical zone protection	first-air and airflow interruption	microbial contamination at open product
ASEP-003	Grade B aseptic background control	room classification and monitoring	contamination during interventions
ASEP-004	Barrier isolator glove integrity	glove leak and port sealing	sterile zone breached
ASEP-005	RABS interventions	door opening and approved aseptic technique	operator-associated contamination
ASEP-006	Aseptic personnel qualification	gowning media fills and aseptic behaviour	unqualified operator contaminates product
ASEP-007	Aseptic gown sterilization	sterility of garments and hold	introduced microbial flora
ASEP-008	Gowning sequence and monitoring	skin coverage and gown breaches	personnel contamination routes
ASEP-009	Aseptic line equipment assembly	sterile boundary and line clearance	uncontrolled opening of fluid path
ASEP-010	Sterile tubing connection	connection integrity and disinfection	bioburden introduced into bulk
ASEP-011	Critical zone airflow visualization	smoke study and dynamic interventions	turbulence drives contaminants toward product
ASEP-012	Environmental monitoring viable air	sampling location and alert/action levels	microbial excursion not detected
ASEP-013	Settle plates and active air sampling	exposure and incubation controls	false clean conditions
ASEP-014	Surface contact/ swab sampling	critical surface map and sanitization	persistent contamination missed
ASEP-015	Nonviable particle monitoring	dynamic particle levels and alarm logic	critical room deterioration overlooked
ASEP-016	Aseptic process simulation / media fill	interventions, line duration and shift coverage	no evidence process can maintain asepsis
ASEP-017	APS incubation and growth promotion	conditions and medium suitability	contaminated simulation read as pass
ASEP-018	Aseptic intervention log	routine and nonroutine interventions	critical events missing from batch review
ASEP-019	Aseptic environmental excursions	link events to batch impact	contaminated batch released
ASEP-020	Disinfectant rotation and contact	efficacy, material and residues	resistant flora/persistent contamination
ASEP-021	Sporicidal application	target spores and contact time	bio-contamination not eradicated
ASEP-022	Operator movement and material flow	unidirectional flow and door discipline	cross-contamination routes
ASEP-023	Closed-system breach decision	compromised connection assessment	false assumption of aseptic protection
ASEP-024	Bioburden prior to final filtration	qualified time/temperature	sterility risk under-assessed

04 | AUTOLOGOUS / ALLOGENEIC CELL THERAPIES

25 distinct assessment topics • 75 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
CGT-001	Patient leukapheresis acceptance	collection identity, viability and sterility	wrong or poor-quality starting cells
CGT-002	Chain of identity (COI)	patient-donor identifiers and barcode checks	wrong-patient cell therapy administration
CGT-003	Chain of custody (COC)	handoff signatures and temperature	untraceable critical material
CGT-004	Donor eligibility screening	infectious disease and health risk	transmissible infection from donor
CGT-005	Incoming cryogenic shipment	shipping excursions and closure	low viability or contamination
CGT-006	Apheresis bag integrity	sterile seal and sample identity	material loss or exposure
CGT-007	Cell isolation / enrichment system	target population purity and recovery	incorrect cell dose/composition
CGT-008	Magnetic-bead cell selection	bead residual and selection efficiency	impurity or altered phenotype
CGT-009	T-cell activation reagent	stimulation amount and time	exhaustion or unintended phenotype
CGT-010	Cell transduction for CAR-T	vector MOI and genomic insertion	variable transduction / safety
CGT-011	Cell expansion bioreactor	growth, metabolite and aseptic conditions	contaminated or under-potent cells
CGT-012	Cell culture medium supplement	cytokine lot and concentration	phenotypic drift or poor proliferation
CGT-013	Cell dose calculation	viable cell concentration and patient weight	underdose or overdose
CGT-014	Cell identity/purity flow cytometry	gating, markers and assay controls	incorrect final cell population
CGT-015	Cell exhaustion and potency assay	phenotypic markers and function	therapy lacks intended activity
CGT-016	Sterility rapid-test decision	sensitivity versus short shelf life	contaminated cells infused
CGT-017	Cell therapy endotoxin control	exposure route and sample volume	pyrogenic reaction
CGT-018	Cell therapy mycoplasma testing	method sensitivity and rapid turnaround	mycoplasma-transmissible product
CGT-019	Cell cryopreservation formulation	DMSO level and cooling ramp	poor recovery or DMSO adverse effects
CGT-020	Controlled rate cell freezing	temperature profile and bag placement	loss of viable cell dose
CGT-021	Cell thawing at clinic	temperature, time and process errors	potency loss immediately before infusion
CGT-022	Cell therapy release under constraints	short shelf life and pending tests	unsubstantiated release decision
CGT-023	Autologous work area segregation	simultaneous patients and equipment	cross-patient mix-up
CGT-024	Cell product transportation to hospital	time/temp, COI and flight disruption	product failure or wrong destination
CGT-025	Cell therapy post-infusion traceability	patient linkage and long-term follow up	late adverse effect not attributable

05 | CELL BANK, SEED LOT & GENETIC STABILITY

22 distinct assessment topics • 66 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
BANK-001	Master cell bank creation	source lineage, clone identity and passage	wrong cell substrate production
BANK-002	Working cell bank generation	MCB to WCB traceability	lot identity or drift error
BANK-003	Research cell bank segregation	GMP versus research stock controls	unqualified research stock used
BANK-004	Master virus seed preparation	virus seed identity and genetic stability	wrong virus strain or adventitious agent
BANK-005	Working virus seed preparation	seed pedigree and passage restrictions	antigen change or unsafe mutation
BANK-006	Bacterial strain reference bank	strain identity and plasmid maintenance	wrong production microorganism
BANK-007	Fungal/yeast seed bank	purity, strain characteristics and identity	cross-strain contamination
BANK-008	Cell bank vial labelling	unique bank ID, clone and passage	vial mix-up and wrong culture
BANK-009	Cryovial closure integrity	leak, vapor penetration and labels	cross-contamination or stock loss
BANK-010	Controlled rate freezing	temperature slope and cryoprotectant	loss of viability/selection bias
BANK-011	LN2 liquid-phase versus vapor storage	cross-contamination and vapor exposure	bank contamination or thaw
BANK-012	Cryofreezer mapping and alarms	temperature and excursion response	bank degradation or total loss
BANK-013	Cell bank inventory two-person verification	retrieval and chain of custody	wrong bank used in inoculum
BANK-014	Cell-bank quarantine and release	testing, QA approval and status	unreleased stock used
BANK-015	Cell bank mycoplasma testing	assay sensitivity and sample representativeness	mycoplasma in manufacturing culture
BANK-016	Cell bank sterility/bioburden testing	bacterial and fungal detection	contaminated seed introduced
BANK-017	Cell bank retrovirus evaluation	cell substrate-specific adventitious risk	viral hazard uncontrolled
BANK-018	Cell bank identity confirmation	DNA fingerprint/sequence and clone phenotype	wrong clone not detected
BANK-019	Cell bank genetic stability study	defined maximum cell age	product quality drift across passages
BANK-020	Cell bank recovery suitability	viability, productivity and morphology	poor seed affects entire batch
BANK-021	Cell bank backup/dual site storage	disaster recovery and supply security	loss of irreplaceable biological material
BANK-022	Cell bank shipping dry shipper	temperature, orientation and identity	degraded or misrouted bank

06 | CHROMATOGRAPHY & RESIN SYSTEMS

28 distinct assessment topics • 84 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
CHROM-001	Protein A capture resin selection	binding capacity, ligand and leachables	poor capture or ligand impurity
CHROM-002	Protein A column packing	bed height, asymmetry and HETP	channeling and impurity breakthrough
CHROM-003	Protein A loading strategy	dynamic binding capacity and flow rate	product loss and HCP carryover
CHROM-004	Protein A elution pH	acid exposure and residence time	aggregation or degradation
CHROM-005	Protein A resin lifetime	cycle count, performance and bioburden	declining impurity clearance
CHROM-006	Protein A leached ligand assay	method sensitivity and resin aging	residual ligand in final product
CHROM-007	Ion exchange column equilibration	pH/conductivity and bed volume	unexpected binding and variants
CHROM-008	Anion exchange flow-through polish	conductivity, DNA/virus removal	residual impurities/viruses escape
CHROM-009	Cation exchange bind/elute	salt gradient and load density	charge variants not removed
CHROM-010	Hydrophobic interaction chromatography	salt exposure and protein stability	aggregation and low recovery
CHROM-011	Size-exclusion chromatography	bed efficiency, sample volume and flow	aggregates not separated
CHROM-012	Mixed-mode chromatography	multivariate salt and pH interactions	unpredictable clearance/selectivity
CHROM-013	Column packing integrity test	HETP/asymmetry acceptance	channeling missed
CHROM-014	Chromatography resin storage solution	biocide concentration and expiry	microbial growth and contamination
CHROM-015	Column cleaning in place	NaOH concentration/contact	carryover or microbial contamination
CHROM-016	Multi-use column sanitization	bioburden and endotoxin controls	cross-batch contamination
CHROM-017	Chromatography skid pump	flow/pulsation and pressure	variable capture or resin damage
CHROM-018	Chromatography UV sensor	calibration and saturation	wrong peak pooling boundaries
CHROM-019	Inline conductivity and pH probes	compensation and drift	uncontrolled gradient or pH
CHROM-020	Valve manifold route and leakage	valve mapping and gasket integrity	wrong pool composition
CHROM-021	Fraction collector / pool criteria	peak integration and decision rules	wrong fractions pooled
CHROM-022	Chromatography buffer supply	correct buffer identity and reserve volume	process interruption or impurity escape
CHROM-023	Resin lot change comparability	ligand density and performance limits	altered impurity clearance
CHROM-024	Resin carryover study	residual host proteins / prior lot	cross-contamination of next batch
CHROM-025	Column pressure limits	flow, viscosity and resin compression	resin cracking or breakthrough
CHROM-026	Chromatography skid software recipe	valid recipe and setpoint access	incorrect separation process
CHROM-027	Chromatography filter at column inlet	particulate load and fouling	pressure and flow variability
CHROM-028	Affinity capture of Fc-fusion product	Fc binding vs variants	inactive species enriched

07 | CLEANROOM / HVAC / FACILITY CONTAINMENT

21 distinct assessment topics • 63 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
HVAC-001	Cleanroom HVAC air handling unit	temperature, RH, supply airflow	environmental excursions affect asepsis
HVAC-002	Terminal HEPA filter integrity	leaks, fit and scan testing	unfiltered contamination reaches cleanroom
HVAC-003	HEPA filter pressure drop	fouling and bypass risk	airflow protection lost
HVAC-004	ISO cleanroom classification	particle limits in operational state	misclassified cleanroom risk
HVAC-005	Cleanroom pressure differential cascade	room-to-room pressure setpoints	contaminated air moves into clean zone
HVAC-006	Airflow visualization/smoke studies	flow paths during equipment/interventions	first air compromised
HVAC-007	Air change rate / recovery time	dilution and classified recovery	persistent contamination after work
HVAC-008	Room temperature distribution	hot spots and sensor placement	open product temperature risk
HVAC-009	Room relative humidity distribution	RH and condensation control	microbial growth or material degradation
HVAC-010	Airlock interlock sequence	door co-open alarms	pressure cascade collapse
HVAC-011	Material pass-through chamber	cleaning and door discipline	material-borne contamination
HVAC-012	Personnel gowning room zoning	dirty/clean transition control	operator microbial transfer
HVAC-013	Biosafety negative-pressure suites	containment direction and fail safe	live agent aerosol escapes
HVAC-014	Biocontainment exhaust HEPA integrity	exhaust filtration and housing leakage	infectious material released
HVAC-015	VHP room decontamination coverage	spore challenge and equipment shadowing	surviving contamination reservoir
HVAC-016	Compressed-air cleanroom point of use	oil, particles and water specification	airborne process contamination
HVAC-017	Facility pest exclusion and envelope	doors, cracks and pest monitoring	bioburden and particulates
HVAC-018	Drain trap / backflow prevention	bioaerosol migration and hydraulic seals	organisms enter graded area
HVAC-019	Aseptic wall/ceiling joint integrity	cleanability and sealant condition	biofilm or particle accumulation
HVAC-020	HVAC alarms and BMS trend record	alert escalation and timestamp integrity	unrecognized environmental drift
HVAC-021	Facility renovation / shutdown restart	requalification and cleaning before reuse	unqualified area used for manufacturing

08 | CLINICAL SAFETY / PHARMACOVIGILANCE

17 distinct assessment topics • 51 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
PV-001	Postmarket safety signal surveillance	adverse event reports and trends	serious adverse event pattern missed
PV-002	Immunogenicity monitoring program	ADA and neutralizing antibody interpretation	unexpected efficacy/safety effects
PV-003	Infusion reaction investigation	lot, rate and cytokine response	unsafe reaction source unidentified
PV-004	Anaphylaxis signal review	formulation excipients and aggregation	repeat severe allergy risk
PV-005	Vaccine adverse event follow-up	lot and causality / reporting rules	vaccine safety signal not acted upon
PV-006	Cell therapy cytokine release syndrome	identity/potency and clinical response	late severe inflammatory harm
PV-007	Cell therapy late-onset malignancy follow-up	vector integration and long-term data	delayed oncogenic risk not detected
PV-008	Gene therapy long-term follow-up	vector persistence and off-target signal	late safety signal not captured
PV-009	Clinical trial deviation impact on product	patient exposure and lot genealogy	unreliable clinical safety attribution
PV-010	Immunogenicity comparability after CMC changes	ADA assay and new lot trends	unrecognized product-related immune change
PV-011	Clinical site product preparation training	reconstitution and administration	ineffective or unsafe dose administered
PV-012	Temperature excursions at clinical site	product stability and clinical viability	damaged biological product infused
PV-013	Patient chain-of-identity incident	clinical and manufacturing handoff	wrong-patient therapy event
PV-014	Product complaint and vigilance interface	traceable lot + case narrative	quality defect not linked to adverse event
PV-015	Recall / field correction effectiveness	patient/hospital notification and reconciliation	unsafe product remains in use
PV-016	Clinical batch retention/traceability	retain samples and lot genealogies	no investigation evidence for serious events
PV-017	Periodic safety update alignment	quality signals and safety reports	regulatory oversight gaps

09 | CONJUGATES, ADCS & HIGH-POTENCY BIOLOGICS

12 distinct assessment topics • 36 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
NAN-001	Antibody drug conjugate linker qualification	reactivity, purity and stability	unstable or immunogenic conjugate
NAN-002	Cytotoxic payload identity and purity	potency and impurity limits	toxic contaminant or wrong payload
NAN-003	Antibody conjugation reaction	pH, temperature and reaction time	wrong drug-to-antibody ratio
NAN-004	Drug-to-antibody ratio (DAR) assay	distribution and method validity	unreliable ADC potency/PK
NAN-005	Free payload clearance	HPLC impurity and limits	excess systemic cytotoxicity
NAN-006	Conjugation solvent residue	organic residuals and exposure	patient toxic exposure
NAN-007	ADC aggregation control	shear and storage	immune reaction and reduced potency
NAN-008	ADC product contact materials	adsorption / extraction and solvent compatibility	unexpected impurities and low yield
NAN-009	High-potency enclosure containment	OEL/OEB and worker exposure	cytotoxic workplace exposure
NAN-010	ADC cleaning validation	high-potency residue and swab recovery	cross-product toxic carryover
NAN-011	ADC occupational waste decontamination	segregation and validated destruction	hazardous contamination of environment
NAN-012	ADC storage and light sensitivity	linker cleavage and temperature	free drug release during shelf life

10 | DRUG SUBSTANCE FORMULATION & BULK HOLDING

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
FORM-001	Protein concentration adjustment	target strength and dilution volumes	incorrect active content
FORM-002	Formulation buffer composition	pH, ionic strength and excipient concentration	stability/potency degradation
FORM-003	Protein aggregation during mixing	shear, order and mixing rate	particles / immunogenicity potential
FORM-004	Protein oxidation control	dissolved oxygen, trace metals and light	chemical variants accumulate
FORM-005	Surfactant addition	polysorbate identity, peroxide and amount	particle formation or aggregation
FORM-006	Sugar cryoprotectant addition	sucrose/trehalose identity and concentration	freeze damage / potency loss
FORM-007	Viscosity control at high concentration	temperature, shear and protein level	poor filling accuracy and delivery
FORM-008	Formulation pH probe control	calibration in low conductivity	wrong pH release decision
FORM-009	Bulk hold temperature	validated hold time and agitation	bioburden or aggregation rise
FORM-010	Bulk sterile storage bag integrity	closure and gamma exposure suitability	loss of sterile boundary
FORM-011	Bulk drug substance freeze/thaw	rate, container and number of cycles	freeze concentration/aggregation
FORM-012	Bulk DS transport between facilities	temperature and chain of custody	unassessed stability excursion
FORM-013	Bulk mixing homogeneous sampling	sampling location and mixing qualification	wrong concentration measurement
FORM-014	Product contact silicone oil	lubricant amount and interaction	protein particulates and aggregation
FORM-015	Bulk transfer line preflush	residue, wetting and product loss	potency loss/contamination
FORM-016	Bacterial endotoxin control	raw material and process water endotoxin	pyrogenicity in patients
FORM-017	Bioburden control prior to formulation	sampling and hold-time acceptance	microbial proliferation
FORM-018	Light-sensitive biologic protection	exposure dose and container	photodegradation
FORM-019	Oxygen headspace control	nitrogen overlay where validated	oxidative degradation
FORM-020	Formulation compatibility with delivery device	syringe/infusion bag/needle	adsorption, clogging or incompatibility

11 | EHS / BIOSAFETY / ENVIRONMENTAL

25 distinct assessment topics • 75 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
EHS-001	Biological agent risk group classification	BSL/containment and agent infectious properties	worker infection or laboratory release
EHS-002	GMO permits and containment review	recombinant organism type and local law	unapproved environmental release
EHS-003	Biosafety cabinet certification	airflow and HEPA performance	operator or sample exposure
EHS-004	Bioreactor aerosol generation control	sampling and vent opening operations	bioaerosol inhalation risk
EHS-005	Fermenter exhaust filter containment	breakthrough and differential pressure	live organism discharge
EHS-006	Chemical inactivation of GMO waste	validated contact time and concentration	viable recombinant waste disposed
EHS-007	Thermal effluent decontamination	temperature/dwell and biological challenge	infectious liquid sent to drain
EHS-008	Sharps injury prevention	needles and biohazard sampling	percutaneous biological exposure
EHS-009	Cell culture cryogenic LN2 hazards	asphyxiation, frostbite and ventilation	serious injury to staff
EHS-010	Liquid nitrogen oxygen monitor	alarm setpoint and sensor calibration	undetected oxygen depletion
EHS-011	Solvent and ethanol storage	flammable concentration and explosion zoning	fire / process loss
EHS-012	High-pressure homogenizer hazards	pressure relief and guarding	mechanical rupture and worker injury
EHS-013	Centrifuge rotor integrity	overspeed, lid interlock and fatigue	rotor failure and injury
EHS-014	Bioreactor pressure vessel safety	pressure relief and certification	pressure incident and hazardous release
EHS-015	Caustic/acid CIP handling	closed chemical dosing and PPE	chemical burns / emissions
EHS-016	Hydrogen peroxide / VHP exposure	safe aeration and occupational limits	oxidative exposure to operators
EHS-017	Formaldehyde vaccine inactivation hazard	ventilation and spill control	toxicity / workplace exposure
EHS-018	Biotoxin / potent payload handling	containment and occupational exposure limits	harmful cytotoxic exposure
EHS-019	Potent biologic segregation	occupational respiratory/dermal limits	sensitization or toxicity
EHS-020	Spill containment in classified area	chemical/biological clean-up and QA assessment	worker exposure / contaminates facility
EHS-021	Safety instrumented interlocks testing	critical pressure and temperature protections	major process safety event
EHS-022	Laboratory infectious waste segregation	labelling and sterilization	infectious waste exposure
EHS-023	Emergency response for infectious releases	spill drills, reporting and medical follow up	expanded incident impact
EHS-024	Environmental permit discharge monitoring	effluent COD/BOD, kill performance and law	unauthorized environmental harm
EHS-025	Ergonomics in cell-processing suites	repetitive manual handling and awkward posture	worker injury / process errors

12 | ENGINEERING / EQUIPMENT MAINTENANCE

25 distinct assessment topics • 75 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
EN-001	Bioreactor agitator seal and motor	vibration, oil leaks and PM	vessel contamination or mechanical failure
EN-002	Fermenter jacket and heat exchanger	temperature transfer and leak testing	thermal excursions / cross-contamination
EN-003	CIP skid pump and sensors	flow, conductivity and temperature	inadequate automated cleaning
EN-004	SIP steam supply control	steam quality and temperature	nonsterile process line
EN-005	Automated valve position indication	feedback and actuator reliability	wrong routing/sterility failure
EN-006	Aseptic diaphragm valve maintenance	diaphragm lifetime and closure	microbial ingress or valve leak
EN-007	Production scales and load cells	calibration and capacity	wrong batch component amount
EN-008	Autoclave / moist heat sterilizer	thermal mapping and air removal	nonsterile parts in process
EN-009	Dry heat sterilizer/depyrogenation	temperature/time and endotoxin kill	endotoxin / bioburden persists
EN-010	Clean steam generator	noncondensable gases, dryness and superheat	sterilization inadequacy
EN-011	Vaporised hydrogen peroxide generator	cycle concentration and aeration	incomplete isolator decontamination
EN-012	Gasket / elastomer preventive replacement	material compatibility and lifetime	contamination or leak
EN-013	Instrument calibration master register	due dates and criticality	GMP CPP readings unreliable
EN-014	Differential pressure transmitters	accuracy and calibration	room cascade failure unnoticed
EN-015	Temperature probes/RTDs	installation, drift and calibration	wrong process control decisions
EN-016	pH/DO instrument calibration	probe lifecycle and 2-point calibration	uncontrolled bioreactor conditions
EN-017	Mass flow controller oxygen/nitrogen	flow calibration and gas identity	culture process variability
EN-018	Emergency power / generator start	outage transition and fuel	culture/sterile environment loss
EN-019	Critical UPS battery autonomy	actual load test and maintenance	equipment uncontrolled shutdown
EN-020	Compressed-gas regulators	material compatibility and filtration	gas contamination / wrong pressure
EN-021	Process equipment weld inspection	surface, crevices and passivation	biofilm or particulates
EN-022	Pump mechanical seal leakage	seal material and inspection	bioburden/chemical cross contamination
EN-023	Maintenance access in cleanrooms	tool transfer and post-work clearance	maintenance introduces contamination
EN-024	Recommissioning after invasive PM	IQ/OQ or risk-based check	equipment used outside qualified status
EN-025	Spare part equivalence	material, grade and supplier approval	unexpected extractables or equipment failure

13 | HR / ADMIN / PERSONNEL COMPETENCY

15 distinct assessment topics • 45 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
HR-001	Biotechnology role competency matrix	molecular biology, asepsis and GMP skill	unqualified person handles critical steps
HR-002	Aseptic gowning qualification	initial/recurrent assessment	microbial contamination from personnel
HR-003	Bioburden sampling competency	sampling technique and timing	unreliable micro results
HR-004	Cell therapy patient identity double-check	training and human factors	wrong patient cells released
HR-005	Bioreactor operator certification	recipe controls and process interventions	culture loss or quality excursion
HR-006	Chromatography operator training	pooling and cleaning proficiency	wrong fraction pooled
HR-007	Analytical bioassay analyst qualification	biological assay variability	incorrect batch potency
HR-008	Biosafety / BSL training	agent-specific containment and PPE	infection or GMO release
HR-009	Access control for cell banks	restricted roles and logs	wrong vial removal/unauthorized access
HR-010	Shift handover in long bioprocesses	CPP changes and deviations	loss of process situational awareness
HR-011	Contractor cleanroom entry	hygiene, escort and tool transfer	critical area contamination
HR-012	Personnel illness reporting	microbial risk and handling restrictions	contaminated product from staff
HR-013	Occupational exposure health program	vaccination and incident response	untreated infectious exposure
HR-014	Emergency drills for LN2 and freezers	evacuation and backup storage	injury or bank loss
HR-015	Training record effectiveness checks	observed qualification and retraining	paper training conceals errors

14 | IT / CSV / AUTOMATION / DATA INTEGRITY

25 distinct assessment topics • 75 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
CSV-001	SCADA bioreactor control logic	validated setpoints, recipes and interlocks	automated culture failure
CSV-002	PLC firmware and configuration	version/patch and change control	unreviewed process control differences
CSV-003	Manufacturing execution system MES	lot genealogy, status and eBR rules	wrong step or lot released
CSV-004	LIMS laboratory sample login	ID, custody and status	sample mix-up or invalid result
CSV-005	Chromatography data system	peak integration and audit trails	manual changes conceal impurities
CSV-006	Bioassay image analysis software	algorithm validation and raw images	incorrect potency measurement
CSV-007	Cell counter software algorithm	thresholds and cell viability	unreliable culture decisions
CSV-008	Sequencing bioinformatics pipeline	version, variant filters and data provenance	misclassified sequence/identity
CSV-009	QPCR/ddPCR analysis software	thresholds, baseline and run approval	incorrect residual DNA/viral results
CSV-010	Automated freezer inventory LIMS	vial position and chain of custody	wrong cell bank retrieved
CSV-011	Environmental monitoring system EMS	data gaps, alarms and location mapping	undetected cleanroom excursions
CSV-012	Building management system BMS	HVAC controls and recipe separation	pressure cascade failure
CSV-013	Historical process data integrity	timestamp, gap controls and retention	critical batch trend cannot be reconstructed
CSV-014	GxP electronic audit trail review	risk-based selection and exception triage	undetected data manipulation
CSV-015	Electronic signatures authorization	identity, meaning and change audit	unapproved disposition appears approved
CSV-016	Computer access provisioning	role and segregation of duties	unauthorized GMP action
CSV-017	Computer backup and restore test	availability and validated restored data	critical quality record lost
CSV-018	Disaster recovery for process control	fail safe, backup site and recovery time	bioprocess interruption and lost traceability
CSV-019	Cybersecurity incident response	ransomware, remote access and reporting	product release records compromised
CSV-020	System validation on cloud migration	data/logic reconciliation and evidence	lost or altered regulated records
CSV-021	Network-connected instrument time sync	NTP and event chronology	unreconstructable deviations
CSV-022	Automated alarm routing validation	SMS/e-mail triggers and escalation	critical environmental excursion missed
CSV-023	ERP supplier lot master data	expiry, GMP release and segregation	unapproved component used
CSV-024	Recipe parameter download	master/slave sync and approval	wrong validated CPP setpoint applied
CSV-025	Software periodic review and obsolescence	patching, access and ongoing fit	undetected system vulnerability or noncompliance

15 | INOCULUM PREPARATION / SEED TRAIN

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
SEED-001	Cell bank thaw in water bath	time, temperature and vial contamination	reduced viability or introduced bioburden
SEED-002	Seed transfer into shake flask	aseptic connection and culture identity	incorrect or contaminated inoculum
SEED-003	Biosafety cabinet for seed handling	airflow protection and disinfection	cross-contaminated culture
SEED-004	Orbital shaker operation	rpm, orbit and CO2 atmosphere	unexpected cell growth phenotype
SEED-005	CO2 incubator control	temperature, CO2, humidity and alarms	pH disturbance and culture stress
SEED-006	Seed medium preparation	concentration, pH and filtration	poor seed performance
SEED-007	Cell density / viability reading	method calibration and representative sample	incorrect inoculum ratio
SEED-008	Seed train culture expansion	passage duration and growth limits	loss of process control
SEED-009	Seed transfer tubing selection	tubing ID and compatibility	leaks, extractables or flow issues
SEED-010	Sterile tube welder/sealer	weld integrity and fusion cycle	open microbial pathway
SEED-011	Aseptic connectors and valves	compatibility and connection verification	contaminated seed train
SEED-012	Seed bioreactor CIP/SIP readiness	cleanliness and sterile path	seed batch bioburden event
SEED-013	Seed bioreactor agitation	shear and oxygen transfer	cell damage and altered CQA
SEED-014	Seed bioreactor dissolved oxygen	probe performance and oxygen delivery	metabolic shift and lost yield
SEED-015	Seed bioreactor pH control	probe drift and base addition	growth and product profile variation
SEED-016	Seed antifoam addition	identity, volume and bioburden	impurity or filter fouling downstream
SEED-017	Seed inoculation hold time	cold/ambient exposure duration	loss of viability and contamination
SEED-018	Seed transfer pressure balancing	positive pressure and airflow	uncontrolled aerosol or backflow
SEED-019	Sampling valve and aseptic sampling	representative sample and closed asepsis	false results or batch contamination
SEED-020	Seed train environmental monitoring	personnel and open operation conditions	undetected contamination route

16 | LABELLING / PACK / SERIALIZATION

18 distinct assessment topics • 54 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
PKG-001	Sterile vials glass compatibility	glass delamination and particle risk	injected glass particles
PKG-002	Elastomer stopper extractables	extractables/leachables and sterilization	protein destabilization or toxicity
PKG-003	Pre-filled syringe barrel interaction	silicone/adhesive and adsorption	protein particle formation
PKG-004	Primary container closure integrity	vial, syringe and cartridge seal	loss of sterility in shelf life
PKG-005	Label master artwork version	strength, INN and storage claim	mislabelled biological dose
PKG-006	Patient-specific CGT label	chain of identity and barcode	wrong-patient infusion
PKG-007	Vaccine lot and expiry code	print readability and release data	wrong or expired vaccine dispensed
PKG-008	Cold-chain shipper exterior instructions	orientation and freezing warnings	temperature damage in transit
PKG-009	Serum batch label verification	lot traceability and version control	wrong bulk placed in use
PKG-010	Biosafety warning/handling label	infectious material classification	unprotected worker exposure
PKG-011	Lyophilized product diluent kit	matched diluent and reconstitution instructions	incorrect preparation/strength
PKG-012	Over-labeling for multiple markets	language, trace and expiry	wrong jurisdictional instructions
PKG-013	Tamper evidence and sealing	access and package integrity	adulteration or mixup
PKG-014	Serialization/track and trace	unique identifiers and aggregation	counterfeit/recall inefficiency
PKG-015	Carton/shipper temperature sensor placement	sensor representation of product	unseen product temperature excursion
PKG-016	Clinical trial blinded labels	randomization and treatment assignment	trial unblinding / wrong treatment
PKG-017	Labelling line clearance	prior label/leaflet removal	cross-product label mix-up
PKG-018	Packaging component supplier change	material and impact assessment	new compatibility or quality risk

17 | LYOPHILIZATION / FREEZE DRYING

24 distinct assessment topics • 72 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
LYO-001	Lyophilizer shelf temperature mapping	uniform shelf response and product temperature	collapse or inconsistent moisture
LYO-002	Lyophilizer condenser capacity	ice capture and batch load	incomplete sublimation
LYO-003	Vacuum pump performance	ultimate pressure and vacuum control	cycle failure and slow drying
LYO-004	Pirani and capacitance manometers	pressure accuracy and calibration	incorrect endpoint decision
LYO-005	Freezing ramp and nucleation	nucleation conditions and ice morphology	nonuniform cake and stability
LYO-006	Annealing step	temperature and hold duration	undesired crystal/pore structure
LYO-007	Primary drying shelf temperature	critical product temperature margin	cake collapse and degraded potency
LYO-008	Primary drying chamber pressure	heat transfer and vapor load	incomplete sublimation
LYO-009	Secondary drying time and temperature	bound water removal	high residual moisture or protein damage
LYO-010	End point determination	comparative pressure / moisture evidence	wet batch released
LYO-011	Chamber sterilization SIP	temperature penetration and load configuration	microbial contamination risk
LYO-012	Lyophilizer chamber leak test	vacuum rise and integrity	loss of sterile boundary
LYO-013	Sterile vent filter integrity	bacteria retention and leaks	nonsterile gas into chamber
LYO-014	Automatic loading/unloading	sterility and vial position	aerodynamic contamination or toppled vials
LYO-015	Manual vial transfer	exposure duration and first air	environmental contamination
LYO-016	Partial stoppering under vacuum	stopper lift and closure	loss of container closure integrity
LYO-017	Nitrogen backfill quality	sterile filter and oxygen/moisture content	product oxidation or contamination
LYO-018	Lyophilizer CIP spray coverage	coverage and residue removal	cross-product carryover
LYO-019	Lyophilizer steam condensate removal	drainage and trapped condensate	inadequate heat penetration
LYO-020	Freeze dryer alarm and abort handling	recovery strategy and excursion management	unjustified product release
LYO-021	Lyophilized cake inspection	cake appearance and vial position	degraded/nonuniform product missed
LYO-022	Reconstitution time and potency	reconstitution conditions and assay	incorrect clinical dose or insolubility
LYO-023	Vial residual moisture testing	Karl Fischer/NIR sampling plan	moisture-driven instability
LYO-024	Lyophilization scale-up	shelf area/loading versus formulation	commercial cycle not comparable

18 | MICROBIAL FERMENTATION

24 distinct assessment topics • 72 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
MICF-001	Inoculum strain verification	strain identity and plasmid carriage	wrong molecule produced
MICF-002	Seed fermenter sterilization in place	sterile boundary and hold time	microbial contamination
MICF-003	Fermenter agitation and impeller	tip speed, shear and mass transfer	low titer or foam events
MICF-004	Fermenter aeration and sparger	oxygen transfer and sterile gas	oxygen starvation or contamination
MICF-005	Fermenter temperature control	heat removal during high respiration	thermal kill or impurity shift
MICF-006	Fermenter pH control	acid/base feed and probe drift	undesired fermentation metabolites
MICF-007	Fermenter oxygen cascade	DO, airflow, rpm and O2 enrichment	culture collapse or byproduct formation
MICF-008	Fermenter overpressure relief	blocked vent and setpoint	vessel damage or aerosol release
MICF-009	Exhaust gas biofilter	integrity and microbial retention	live organism release to environment
MICF-010	Foam-breaker and antifoam	foam control and downstream compatibility	broth overflow or process fouling
MICF-011	Carbon source feed pump	feeding concentration and rate	overflow metabolism and lower yield
MICF-012	Induction chemical addition	inducer identity, dose and timing	protein expression failure
MICF-013	Plasmid selection marker control	plasmid retention and antibiotic use	loss of intended construct
MICF-014	Fermentation contamination trending	routine Gram stain and bioburden	competing microorganism obscured
MICF-015	Endotoxin accumulation control	gram negative biomass and purification burden	unacceptable endotoxin in final product
MICF-016	Harvest at defined phase	biomass, expression and viability indicators	proteolytic damage or low potency
MICF-017	Fermenter decontamination after batch	validated kill and discharge criteria	live recombinant organism release
MICF-018	High-cell-density fermentation	oxygen/heat and viscosity control	heterogeneous growth and impurity increase
MICF-019	Fermentation exhaust condensate	aerosol condensation and filters	cross-contamination or biosafety exposure
MICF-020	Fermenter sampling valve	sample sterility and containment	contamination or operator exposure
MICF-021	Protein inclusion body formation	induction temperature and redox	misfolded/aggregated protein
MICF-022	Yeast methanol induction	flammability and feed accuracy	fire or uncontrolled expression
MICF-023	Fungal fermentation morphology	pellet size and viscosity	mass-transfer variability and yield loss
MICF-024	Fermentation downstream transfer	line pressure, status and kill-valve control	uncontrolled transfer or containment loss

19 | MICROBIOLOGY / STERILITY / ADVENTITIOUS QC

21 distinct assessment topics • 63 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
MICQC-001	Sterility testing isolator qualification	decontamination and glove integrity	false sterility results
MICQC-002	Sterility test membrane filtration	product interference and membrane suitability	missed contaminants in product
MICQC-003	Sterility test direct inoculation	growth inhibition and hold conditions	false negative microbial growth
MICQC-004	Rapid microbiological sterility methods	validation and detection limits	contaminated short-life product released
MICQC-005	Growth promotion test	challenge organisms and inoculum	invalid negative test results
MICQC-006	Media fill laboratory incubation	time/temperature and reading	contaminated process simulation accepted
MICQC-007	Bioburden membrane filtration assay	volume, recovery and interference	high microbial load goes unnoticed
MICQC-008	Environmental monitoring trend analysis	site flora and alert/action levels	emerging persistent contamination undetected
MICQC-009	Cleanroom surface recovery methods	swab/contact plate suitability	surface contamination underestimated
MICQC-010	Aseptic operator gown monitoring	sample site, recovery and timing	poor aseptic behaviour missed
MICQC-011	Facility isolate identification	MALDI/sequence and critical isolates	contamination source unknown
MICQC-012	Bacterial endotoxin testing	MVD/inhibition enhancement	unsafe endotoxin accepted
MICQC-013	Mycoplasma culture detection	fastidious culture capability	mycoplasma contamination missed
MICQC-014	Mycoplasma NAT validation	sample matrix and positive controls	false-negative culture results
MICQC-015	Adventitious virus assay cell culture	indicator cells and assay duration	unrecognized infectious agent
MICQC-016	PCR contamination controls	segregated pre/post amplification	false positive source investigation
MICQC-017	Microbial identification media expiry	medium qualification and storage	incorrect species attribution
MICQC-018	Incubator mapping and alarms	temperature uniformity and excursion	growth detection compromised
MICQC-019	Biosafety cabinet airflow certification	HEPA and inflow/downflow rates	test cross contamination / exposure
MICQC-020	Microbiology sample chain of custody	sample integrity and storage	false batch conclusion
MICQC-021	Growth-based test data integrity	original observations, IDs and photos	suppressed positive test outcomes

20 | PLASMA-DERIVED BIOLOGICALS

16 distinct assessment topics • 48 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
PLASMA-001	Plasma donor eligibility	screening and collection eligibility	transfusion-transmissible agent risk
PLASMA-002	Plasma unit ID and pooling	donor traceability and exclusion	untraceable contaminated pool
PLASMA-003	Plasma transport frozen chain	minimum temperature and excursion	protein degradation/contamination
PLASMA-004	Plasma thaw control	time and target temperature	protein denaturation and microbial risk
PLASMA-005	Cold ethanol fractionation	ethanol concentration, pH and temperature	wrong protein separation
PLASMA-006	Fractionation vessel explosion protection	flammable ethanol vapor and ignition	major fire and product loss
PLASMA-007	Fractionation centrifuge	separation efficiency and containment	cross-fraction impurities
PLASMA-008	Plasma pool viral NAT testing	assay sensitivity and pool sampling	infectious donations undetected
PLASMA-009	Plasma viral inactivation step	validated reduction and process conditions	infectious agent carryover
PLASMA-010	Plasma nanofiltration step	filter retention and pressure	residual viruses escape
PLASMA-011	Solvent-detergent removal	chemical residues and validation	toxic chemical exposure
PLASMA-012	Albumin purity and aggregate testing	HPLC/electrophoretic quality profile	unsafe protein aggregates
PLASMA-013	Immunoglobulin IgG fragment/aggregate	monomer profile and assay	immune side effects
PLASMA-014	Thrombotic agent risk in immunoglobulin	coagulation factor contaminants	adverse thrombotic events
PLASMA-015	Plasma source traceability retention	donor database and notification	ineffective look-back investigation
PLASMA-016	Plasma fractionation cleaning	carryover of protein and ethanol	cross contamination between pools

21 | PLASMID DNA / GENE EDITING

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
PLAS-001	Plasmid host-strain authenticity	sequence and bacterial cell bank	wrong plasmid DNA identity
PLAS-002	Plasmid fermentation selection pressure	selection agent and copy number	loss of plasmid or variants
PLAS-003	Plasmid supercoiled fraction	topology and impurity specification	reduced transfection potency
PLAS-004	Plasmid genomic DNA removal	chromosomal DNA impurity assay	unwanted DNA exposure
PLAS-005	Plasmid endotoxin clearance	LPS removal and lot suitability	pyrogenic patient response
PLAS-006	Plasmid antibiotic-resistance gene concern	sequence, residual marker and assessment	unjustified resistance marker exposure
PLAS-007	Plasmid DNA precipitation	alcohol/salt levels and recovery	degraded or impure DNA
PLAS-008	Plasmid chromatography purification	resin/gradient and isoform separation	open circular/linear DNA carryover
PLAS-009	Plasmid residual RNA and proteins	RNase and purification performance	impurity profile out of control
PLAS-010	Plasmid sterile drug substance storage	DNA integrity and freeze/thaw cycles	loss of biological activity
PLAS-011	CRISPR guide RNA design	off-target analysis and on-target efficiency	unwanted genomic edits
PLAS-012	Cas nuclease raw material quality	protein activity, endotoxin and purity	undesired edit or toxicity
PLAS-013	Genome edit delivery mode	electroporation/lipid/vector suitability	cell viability decline
PLAS-014	Editing process verification	on-target sequence and allele distribution	incorrect edited product
PLAS-015	Off-target edit monitoring	method sensitivity and sampling	late genotoxic effect overlooked
PLAS-016	Residual gene editing reagents	Cas/guide residual assay	unintended persistent editing
PLAS-017	Gene edited clone selection	genetic stability and clonal heterogeneity	unstable intended phenotype
PLAS-018	Gene edited cell manufacturing expansion	passage/cell state and potency	loss of edited phenotype
PLAS-019	Genome integrity testing	structural variants and translocations	genomic safety hazard
PLAS-020	Nucleic acid batch sequence release	NGS identity and analysis controls	mismatched gene therapy material

22 | PRIMARY HARVEST / CLARIFICATION

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
HAR-001	Culture harvest timing	viability and protease release threshold	product degradation during harvest
HAR-002	Harvest transfer pump	shear, speed and seal integrity	protein aggregation and leakage
HAR-003	Harvest cooling exchanger	cooling rate and temperature	protease activity or loss of potency
HAR-004	Disc-stack centrifuge feed	g-force, residence time and balance	incomplete solids removal
HAR-005	Centrifuge bowl seal	aerosol containment and integrity	open microbial pathway or exposure
HAR-006	Continuous centrifuge interface	clarity and turbidity setpoint	solids breakthrough into downstream
HAR-007	Depth filter train sizing	capacity, flux and fouling endpoints	filter bypass or productivity loss
HAR-008	Depth filter media compatibility	extractables and product adsorption	product loss or leachables
HAR-009	Harvest filter differential pressure	pressure limits and membrane integrity	breakthrough or filter failure
HAR-010	Harvest hold tank	hold time, temperature and mixing	bioburden/proteolysis rise
HAR-011	Cell lysis method selection	chemical/mechanical release and impurity burden	DNA/HCP contamination load
HAR-012	High-pressure homogenizer	pressure, cycle count and cooling	excess protein damage or incomplete lysis
HAR-013	Microfluidizer disruption	thermal/shear exposure and passes	protein denaturation
HAR-014	Harvest clarification sampling	representative turbidity and impurity level	uncontrolled solids carryover
HAR-015	Harvest transfer line clearance	batch identity and line integrity	cross-batch contamination
HAR-016	Harvest closed manifold routing	valve state and hose line-up	wrong destination tank filled
HAR-017	Protein A bind feed pretreatment	pH, conductivity and aggregates	poor affinity capture and fouling
HAR-018	Bioreactor to clarification scheduling	maximum hold and equipment readiness	bulk quality decline while waiting
HAR-019	Harvest bag fill/volume limits	weight, pressure and headspace	leak or uncontrolled spillage
HAR-020	Centrifuge cleaning verification	residual cells and bioburden	cross-batch carryover

23 | PURCHASE / SUPPLIER / OUTSOURCING

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
PUR-001	Supplier qualification of cell culture media	composition control, origin and change notices	uncontrolled media affects CQA
PUR-002	Supplier quality agreement	release, investigation and communication	unclear quality responsibility
PUR-003	Resin supplier qualification	functional capacity and extractables changes	unanticipated DSP impurity profile
PUR-004	Single-use film supplier	polymer grade and irradiation	new leachables or failure of bags
PUR-005	Sterile connector supplier	sterility assurance and component fit	aseptic transfer failure
PUR-006	Sterilizing filter supplier	retention grade and change control	unverified bacteria retention
PUR-007	Cell bank storage service provider	alarm reliability and disaster recovery	critical cell banks lost
PUR-008	Plasmid/GMP-grade DNA vendor	sequence/identity and impurity	incorrect genetic input
PUR-009	Viral vector outsourced CMO	process/containment and traceability	uncontrolled vector safety
PUR-010	Contract fill-finish supplier	aseptic process validation and controls	sterility assurance gaps
PUR-011	Contract testing laboratory	method transfer, audits and data integrity	invalid release results
PUR-012	Cold chain 3PL supplier	lane qualification and excursion actions	temperature damaged product
PUR-013	Clinical courier qualification	chain of identity and customs	wrong or delayed cell therapy
PUR-014	Excipient supplier qualification	bioburden, endotoxin and peroxide controls	protein instability or pyrogenicity
PUR-015	Animal-origin material supply	TSE/BSE and traceability	infectious agent introduction
PUR-016	Critical electronic system supplier	software support and lifecycle	uncontrolled validated system change
PUR-017	Reference standard source supplier	assigned potency and traceability	assay calibration bias
PUR-018	Approved vendor list status control	audit and complaint tracking	blocked supplier inadvertently used
PUR-019	Procurement specification change review	technical and QA impact	unapproved raw material substitution
PUR-020	Supplier business continuity	sole source critical component and inventory	production interruption / rushed changes

24 | QA / QUALITY MANAGEMENT SYSTEM

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
QA-001	Batch review and certification	critical records, exceptions and release criteria	affected biological batch released
QA-002	Deviation and event triage	criticality and product impact escalation	uninvestigated process excursions
QA-003	CAPA root cause effectiveness	recurrence evidence and verification	same failure repeats across batches
QA-004	Change control assessment	product and process comparability triggers	unassessed process drift affects quality
QA-005	Complaint investigation	market quality and product traceability	latent product defect not detected
QA-006	Recall and mock recall	lot genealogy and authority notification	impacted lots remain distributed
QA-007	Internal GMP audit planning	risk-based frequency and scope	critical compliance gaps persist
QA-008	Supplier audit qualification	critical outsourced GMP process controls	external contamination not prevented
QA-009	Quality agreement governance	testing, storage, cell bank, fill-finish roles	release accountability unclear
QA-010	Annual product quality review/PQR	trending CPP, CQA, impurities and deviations	emerging drift overlooked
QA-011	Out-of-specification investigations	validity and quality impact decision	false OOS rejection or unsafe release
QA-012	Out-of-trend investigation	subtle potency and impurity trends	process deterioration missed
QA-013	Data integrity program	ALCOA+, audit trails and original records	unreliable lot disposition evidence
QA-014	Document control and issuance	approved master records and revisions	uncontrolled process instruction used
QA-015	GMP training qualification	aseptic and biosafety role performance	operator error contamination
QA-016	Reference/retention sample program	traceability and representative retains	no reliable future investigation sample
QA-017	Quality culture and speak-up escalation	timely process deviation reporting	undocumented correction hides defects
QA-018	Site quality council oversight	resource allocation and KPI escalation	critical issues delayed
QA-019	Contract laboratory governance	method transfer and data verification	invalid third party release results
QA-020	Product quality defect trend review	signals by site and product	early safety signal missed

25 | QC ANALYTICAL / BIOASSAY LABORATORY

34 distinct assessment topics • 102 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
QC-001	HPLC reversed-phase protein purity	column resolution and system suitability	protein impurity overlooked
QC-002	SEC-HPLC aggregate assessment	column/method stability and recovery	high-molecular weight species missed
QC-003	IEX-HPLC charge variant assay	pH/gradient and peak integration	changed deamidation/charge profile missed
QC-004	CE-SDS reduced/nonreduced method	separation and sample denaturation	fragment or disulfide variant missed
QC-005	Capillary isoelectric focusing	pI calibration and ampholytes	charge variants mischaracterized
QC-006	LC-MS peptide mapping	mass accuracy and digestion completeness	wrong sequence or modification overlooked
QC-007	Intact mass spectrometry	deconvolution and reference standards	incorrect molecular species accepted
QC-008	Glycan profiling by HILIC	labelling efficiency and calibration	altered glycosylation undiscovered
QC-009	N-terminal sequencing	sample purity and analytical sensitivity	product identity error
QC-010	Amino acid composition analysis	hydrolysis and standardization	incorrect protein quantity claim
QC-011	Protein assay UV280	extinction coefficient and path length	incorrect concentration assignment
QC-012	Potency cell-based reporter assay	cell passage, assay parallelism and controls	ineffective drug lot released
QC-013	ADCC functional potency assay	effector-cell variability and reference	effector function loss undetected
QC-014	CDC complement activity assay	complement quality and signal range	functional change overlooked
QC-015	Binding ELISA	specificity, matrix and standard curve	falsely high binding potency
QC-016	Surface plasmon resonance binding	chip immobilization, kinetics and controls	affinity drift not detected
QC-017	Biolayer interferometry	sensor loading and assay model	inaccurate binding kinetics
QC-018	qPCR residual host-cell DNA	primer/probe recovery and contamination	residual DNA underestimated
QC-019	HCP ELISA	antibody coverage and matrix interference	host-cell proteins in product
QC-020	Protein A leachate assay	sensitivity and specificity	ligand impurity accepted
QC-021	Mycoplasma PCR assay	inhibition, specificity and controls	false negative mycoplasma
QC-022	Residual antibiotic assay	method specificity and limit	allergenic antimicrobial residue
QC-023	Osmolality meter	calibration and sample volume	incorrect osmolality release
QC-024	pH meter for protein bulk	electrode suitability and calibration	unstable protein formulation accepted
QC-025	Karl Fischer moisture test	reagent blank and recovery	wet lyophilized product accepted
QC-026	Endotoxin LAL kinetic chromogenic	inhibition/enhancement and dilution	pyrogenic product falsely passes
QC-027	Rapid endotoxin recombinant factor C	method suitability and interference	invalid endotoxin measurement
QC-028	Titration of formulation components	endpoint and standard normality	wrong excipient concentration
QC-029	ICP-MS trace metals	matrix and sensitivity	catalytic metal impurity undetected
QC-030	Reference standards lifecycle	qualification, storage and expiry	all potency/assay results biased
QC-031	Laboratory electronic data acquisition	raw data audit trail and backup	unreliable QC batch disposition
QC-032	Instrument calibration/qualification	IQ/OQ/PQ and performance checks	invalid critical analytical result
QC-033	QC analyst training and second check	critical method technique and review	repeatable analyst-specific assay bias
QC-034	Sample stability in testing	hold duration and storage condition	sample degradation mistaken for batch defect

26 | QUALITY ASSURANCE / RISK GOVERNANCE

16 distinct assessment topics • 48 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
QRM-001	Quality risk management SOP	defined QRM decision flow and governance	inconsistent risk-based quality decisions
QRM-002	Risk management master plan	scope, criteria, review intervals	systemic gaps in identified critical risks
QRM-003	Quality risk assessment initiation	trigger and impact boundary	quality change implemented without risk review
QRM-004	Risk team multidisciplinary competence	QA, manufacturing, QC, engineering input	unrecognized cross-functional failure pathways
QRM-005	Risk scoring scale qualification	severity, occurrence, detectability definitions	noncomparable scores mask severe risks
QRM-006	Critical quality attributes mapping	identity, purity, potency, safety and stability	uncontrolled CQA threatens efficacy
QRM-007	Critical process parameter mapping	CPP identification and ranges	process drift escapes control strategy
QRM-008	Risk-control hierarchy and effectiveness	preventive safeguards and verification	controls documented but ineffective
QRM-009	High-severity escalation	patient safety and contamination triggers	serious quality risks remain unresolved
QRM-010	Risk acceptance and justification	scientific rationale and signature	unacceptably high residual risks accepted
QRM-011	Annual QRM program effectiveness	trends, signals and overdue risk actions	QRM fails to evolve with experience
QRM-012	Product platform risk mapping	mAb, vaccine, enzyme, vector, cell therapy differences	wrong platform controls reused
QRM-013	Site-wide contamination risk map	cross-product contamination pathways	unrecognized contamination transfer
QRM-014	QRM linkage to quality agreements	outsourced and client obligations	important control has no accountable owner
QRM-015	Benefit-risk decision for investigational biologics	clinical stage and supply limitations	unstated trade-offs in quality acceptance
QRM-016	Risk-file governance and audit trail	traceability from hazard to closure	lost evidence of risk justification

27 | R&D / CELL SUBSTRATE DEVELOPMENT

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
RD-001	Target product profile definition	therapeutic indication and expected CQA	development misses clinical quality needs
RD-002	Expression construct sequence verification	coding region and vector integrity	incorrect biologic identity
RD-003	Promoter / gene regulation selection	expression stability and control	variable or harmful product formation
RD-004	Host cell line selection	genetic stability and adventitious agent burden	unstable or unsafe manufacturing cell line
RD-005	Transfection/recombination strategy	clone identity and off-target changes	inconsistent product quality
RD-006	Single cell cloning evidence	clonality and traceable selection	heterogeneous master cell bank
RD-007	Clone screening high-throughput platform	productivity versus glycosylation quality	poor-quality clone scaled up
RD-008	Cell-line genetic drift assessment	passage limits and sequence stability	loss of potency / new impurities
RD-009	Protein folding and aggregation design	native structure and disulfide integrity	increased immunogenicity
RD-010	Glycosylation development	glycan profiles and effector function	altered PK or biological activity
RD-011	Cell culture media development	raw material variability and nutrients	inconsistent protein expression
RD-012	Feed strategy development	metabolites, osmolality and timing	undesired glycoforms or degradation
RD-013	Upstream scale-down model	representativeness of large-scale process	invalid experimental conclusions
RD-014	Downstream scale-down model	impurity clearance representativeness	unpredicted commercial impurities
RD-015	Analytical method development linkage	CQA method sensitivity and specificity	critical attribute not monitored
RD-016	Reference standard characterization	orthogonal identity and activity assignment	unreliable assay calibration
RD-017	Design-space proposal	proven acceptable range and interactions	out-of-space operation accepted
RD-018	Early formulation screening	protein stability in excipients	aggregation during storage
RD-019	Developability assessment	viscosity, particulates and oxidation	process or delivery unsuitability
RD-020	Process robustness / DoE design	edge of failure and interactions	critical variation not characterized

28 | RAW MATERIALS, MEDIA AND BUFFERS

22 distinct assessment topics • 66 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
MEDIA-001	Chemically defined medium selection	source, impurity and nutrient profile	variable cell growth and product glycosylation
MEDIA-002	Animal-origin component risk assessment	TSE/BSE and adventitious agent controls	transmissible agent introduced
MEDIA-003	Serum supplier qualification	donor herd, geography and testing	viral/mycoplasma contamination
MEDIA-004	Hydrolysate lot variability	amino acid and trace element profile	undesired product variants
MEDIA-005	Raw material trace element variation	copper, manganese and iron ranges	oxidation and glycosylation shift
MEDIA-006	Single-use bag media preparation	material compatibility and closure integrity	leachables or bioburden
MEDIA-007	Media powder weighing	weight, dust control and identity	wrong medium concentration or mix-up
MEDIA-008	Media mixing vessel impeller	homogeneity and mix time	concentration gradients
MEDIA-009	Media adjustment of pH	pH probes, titrants and hold limits	growth or folding deviation
MEDIA-010	Media prefiltration stage	particle removal and differential pressure	filter blockage / particulate carryover
MEDIA-011	0.22 micron sterilizing grade media filter	validated bacteria retention and integrity	contaminated medium enters culture
MEDIA-012	Bioburden prior to sterilizing filter	upstream contamination load	excessive bioburden challenges filters
MEDIA-013	Buffer preparation vessel	chemical composition and mixing	column performance and purity variation
MEDIA-014	Buffer conductivity check	salt concentration and calibration	binding/elution control failure
MEDIA-015	Buffer expiry and maximum hold	age, temperature and growth risk	microbial contamination in solutions
MEDIA-016	Buffer transfer hoses	line clearance, label and assembly	wrong buffer charged to step
MEDIA-017	WFI/PW as process ingredient	microbial/endotoxin and conductivity	endotoxin or microbes enter bulk
MEDIA-018	Media and buffer container ID	identity/barcodes and lot assignment	untraceable source material in product
MEDIA-019	Bio-based antifoam qualification	microbial and extractables properties	adventitious agents or downstream fouling
MEDIA-020	Raw material sampling under containment	representative and aseptic sampling	material contamination or sampling error
MEDIA-021	Protein-free medium transition	comparability of quality profile	unexpected immunogenicity risk
MEDIA-022	Buffer concentration inline dilution	mixing response and flow ratio	incorrect purification gradient

29 | REGULATORY AFFAIRS / CMC

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
REG-001	Biological product jurisdictional classification	vaccine, protein, CGT and biosimilar pathway	wrong licensing and GMP route
REG-002	US BLA/IND applicability	CBER/CDER center and indication	incomplete US authorization strategy
REG-003	India CDSCO manufacturing licence	biological product permissions and site scope	unauthorized manufacture
REG-004	India NDCTR 2019 clinical permission	clinical development and investigational product	noncompliant clinical supply
REG-005	EU marketing authorization route	centralised product category and variation	unapproved CMC commitments
REG-006	EU ATMP GMP Part IV applicability	cell and gene therapy regulatory route	inappropriate conventional GMP assessment
REG-007	Australia TGA ARTG registration	sponsor and evidence obligations	noncompliant distribution
REG-008	UK MHRA licensing	manufacturer/IMP and biologics scope	market authorization gap
REG-009	Quality overall summary / CTD Module 3	cell substrate, controls and process validation	unsubstantiated quality dossier
REG-010	Control strategy change reporting	variation/annual report classifications	changes introduced without authorization
REG-011	Process comparability package	pre/post-change analytical and functional evidence	clinically meaningful product change
REG-012	Reference standards and potency claims	assigned units and methods in dossier	misstated product strength
REG-013	Viral safety dossier	cell substrate testing and clearance justification	unaddressed adventitious agents
REG-014	Adventitious agent testing requirements	species and product-specific panels	infectious agent assurance inadequate
REG-015	Cell bank characterization filing	origin, history and genetic stability	unclear cell substrate suitability
REG-016	Biosimilar regulatory bridging	critical analytical/functional similarity	unsupported biosimilarity claim
REG-017	Labelling/SmPC/PI/IFU control	storage, preparation, route and warnings	unsafe product handling by users
REG-018	Annual report and periodic updates	CMC changes, trends and regulatory deadlines	unreported regulatory changes
REG-019	Biological standard and pharmacopeia applicability	monograph and validated alternatives	invalid release specifications
REG-020	Clinical trial supply import/export	permits, customs and chain of identity	investigational product misrouted

30 | SINGLE-USE SYSTEMS / BIOPROCESS ASSEMBLIES

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
SUS-001	Single-use bioreactor bag supplier	resin and film formulation change control	new extractables in product
SUS-002	Single-use mixing bag fitment	support vessel geometry and load	bag rupture or volume error
SUS-003	Single-use tubing weld specification	fusion temperatures and diameter	weak weld or occlusion
SUS-004	Sterile aseptic connector selection	gender, size, sterility claim	open connection contamination
SUS-005	Tubing pinch/clamp control	closure force and flow path	leak, pressure or misrouting
SUS-006	Peristaltic pump tubing compatibility	fatigue, shedding and extractables	particles/leachables in bulk
SUS-007	Disposable manifold assembly drawing	flow path and valve labels	incorrect process routing
SUS-008	Single-use bag pressure rating	fill volume and pressure surges	catastrophic bag rupture
SUS-009	Sterile transfer set integrity test	preuse leaks and visual checks	contamination introduced during transfer
SUS-010	Presterilized assembly CoA review	irradiation dose and sterility assurance	supplier sterilization failure unnoticed
SUS-011	SUS gamma-aging and shelf life	mechanical strength and extractable aging	expired assembly compromises batch
SUS-012	Film contact extractable/leachable study	product contact, time and temperature	toxic leachables or protein destabilization
SUS-013	SUS sensor calibration	optical DO and single-use pH offsets	wrong bioreactor feedback
SUS-014	SUS particulate inspection	film shedding and weld debris	visible/subvisible particulate in product
SUS-015	Single-use sensor port connection	gasket fit and movement	loss of sterile boundary
SUS-016	Disposable cell-culture bag shipping	folding, abrasion and transit damage	latent leakage during culture
SUS-017	SUS leak testing method	sensitivity and worst-case pressure	small leaks remain undetected
SUS-018	Sterile welding after hold	cut end age and aseptic positioning	bioburden at weld site
SUS-019	SUS waste treatment	live culture bag disinfection and handling	biosafety exposure and GMO release
SUS-020	SUS component lot traceability	resin, film, assembly and irradiation lots	uncertain product impact after supplier defect

31 | STABILITY / COLD STORAGE & CCIT

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
STAB-001	Drug substance stability protocol	long-term and accelerated design	unjustified DS expiry
STAB-002	Drug product real-time stability	storage and expiry claims	degraded commercial product supplied
STAB-003	In-use stability and reconstitution	reconstitution conditions/time	unsafe ineffective dose at administration
STAB-004	Accelerated stress stability	photolysis, agitation and thermal stress	unknown degradation route
STAB-005	Freeze-thaw stability	cycle number and concentration	aggregation after transfer
STAB-006	Shipper excursion study	transport temperature and shock	degradation during distribution
STAB-007	Stability chamber temperature mapping	uniformity and door opening	invalid shelf life evidence
STAB-008	Stability chamber RH mapping	humidity and sensor drift	inconsistent product aging
STAB-009	Stability-indicating potency test	biological assay and trend control	activity loss overlooked
STAB-010	High molecular weight species trending	aggregation and assay sensitivity	immunogenicity risk not assessed
STAB-011	Subvisible particle stability trend	MFI/HIAC and storage effect	particles accumulate in marketed batch
STAB-012	Leachables during shelf life	stopper/glass/syringe interaction	toxic or destabilizing leachables
STAB-013	Container closure integrity over aging	CCI test sensitivity and timepoints	sterility lost late in shelf life
STAB-014	Stopper compatibility and adsorption	silicone/extractables and stability	reduced potency or impurity increase
STAB-015	Cell therapy cryogenic expiration	cell viability and potency over storage	underpotent cells infused
STAB-016	Vaccine freeze damage assay	freezing and adjuvant flocculation	antigen potency reduced
STAB-017	Photostability packaging selection	light exposure and package transmittance	light degraded product
STAB-018	Stability OOT threshold	statistical trend and meaningful shift	progressive degradation not escalated
STAB-019	Reference retain sample handling	sampling and custody at intervals	invalid trend investigation
STAB-020	Stability data statistical evaluation	regression/model assumptions	unjustified shelf life conclusion

32 | TECHNOLOGY TRANSFER / SCALE-UP / CPV

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
TECH-001	Process description knowledge transfer	critical inputs, output and limits	receiver unaware of sensitive parameter
TECH-002	Scale-up bioreactor oxygen transfer	kLa and cell metabolism	product CQA changes at commercial scale
TECH-003	Scale-up agitation/shear	impeller scale and tip speed	cell viability or aggregation shift
TECH-004	Scale-up mixing time	pH/base pulse gradients	charge variant and glycan changes
TECH-005	Scale-up heat transfer	bioreactor thermal gradients	culture growth variability
TECH-006	Seed-train expansion schedule	age, viability and inoculum ratio	process inconsistency in transfer
TECH-007	Chromatography column scale-up	bed height, flow and loading	changed clearance/purity performance
TECH-008	UF/DF membrane surface scale-up	membrane area and TMP	different yield or aggregate levels
TECH-009	Transfer of aseptic filling line	equipment and intervention comparability	unqualified sterility assurance
TECH-010	Transfer of lyophilization cycle	vial loading/geometry and shelf performance	incomplete drying at new site
TECH-011	Transfer of potency bioassay	inter-lab reproducibility and standards	inconsistent strength across sites
TECH-012	Tech transfer analytical comparability	orthogonal CQA methods	subtle change not detected
TECH-013	Transfer cell bank transport	cell identity, viability and shipping	wrong or degraded seed at receiver
TECH-014	Process transfer change control	regulatory commitments and stage gate	unauthorized CMC change
TECH-015	Transfer validation/PPQ strategy	representative worst cases and batches	unproven receiving site capability
TECH-016	Continued process verification	CQA and CPP trends following transfer	late drift not caught
TECH-017	Comparability after media supplier change	raw material sensitivity	shifted glycoform/potency profile
TECH-018	Comparability after bioreactor bag change	extractables/mixing and sensors	unrecognized CQA or leachable shift
TECH-019	Analytical similarity for process changes	biological function vs purity	clinically meaningful shift overlooked
TECH-020	Product lifecycle control strategy update	knowledge management and postapproval	control gaps after transfers

33 | UF/DF, FILTRATION & CONCENTRATION

22 distinct assessment topics • 66 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
TFF-001	TFF cassette selection	MWCO and protein adsorption	product loss or impurity breakthrough
TFF-002	TFF membrane lot variability	flux, selectivity and integrity	inconsistent concentration
TFF-003	TFF skid pressure control	TMP, feed and retentate pressure	membrane damage or aggregation
TFF-004	TFF recirculation pump shear	flow, pump type and exposure time	protein denaturation
TFF-005	TFF concentration endpoint	volume and protein concentration	out-of-target drug substance concentration
TFF-006	Diafiltration exchange volume	diavolumes and residual salt	wrong final formulation buffer
TFF-007	TFF hold temperature	cooling and operation duration	bulk degradation
TFF-008	TFF cassette leak testing	membrane and gasket integrity	bypass or biological contamination
TFF-009	TFF system sanitization	NaOH or approved agent exposure	carryover or bioburden
TFF-010	Membrane cleaning / reuse	residual proteins and fouling	cross-batch contamination
TFF-011	TFF pressure transmitter calibration	TMP accuracy	process operated outside validation
TFF-012	NFF microfiltration membranes	pore ratings and flow capacity	particulate or microbe breakthrough
TFF-013	Sterilizing-grade filter bacteria retention	product matrix and challenge evidence	failure to assure sterile filtrate
TFF-014	Sterile filter preuse integrity test	PUPSIT feasibility and approved approach	filter damage undetected prefiltration
TFF-015	Sterile filter postuse integrity test	bubble point/diffusive flow and acceptance	undetected microbial retention failure
TFF-016	Sterile filtration pressure/flow limit	product-specific validated maximum	filter integrity compromised
TFF-017	Bioburden before sterile filtration	feed bioburden/endotoxin and hold	excess microbial challenge to filter
TFF-018	Filter compatibility with protein formulation	binding, aggregation, extractables	low potency or new impurities
TFF-019	Filter train wrong line-up	flow direction and valves	unfiltered material bypasses barrier
TFF-020	Filter flush and wetting agent	residual fluid and product dilution	unintended formulation change
TFF-021	Retention sample postfiltration	representative sample and sterility	false release data
TFF-022	Deadleg and holdup-volume control	residual volume and dwell time	microbial buildup or product loss

34 | UPSTREAM MAMMALIAN CELL CULTURE

26 distinct assessment topics • 78 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
UPM-001	Stainless bioreactor vessel integrity	surface finish, welds and leak tightness	biofilm or cross-batch contamination
UPM-002	Single-use bioreactor bag integrity	seams, welds and pinholes	leak or environmental contamination
UPM-003	Bioreactor mechanical agitation	rpm, tip speed, shear and mixing	cell damage or aggregation
UPM-004	Bioreactor sparger oxygen transfer	bubble size, dissolved oxygen and kLa	oxygen limitation and glycan variation
UPM-005	Bioreactor carbon dioxide stripping	pCO2 and gas flow balance	undesired metabolism and CQA shift
UPM-006	Bioreactor pH cascade	pH electrode and acid/base dosing	product charge variant shift
UPM-007	Bioreactor temperature loop	thermal overshoot/undershoot	viability and folding changes
UPM-008	Bioreactor load cells	media/feed mass accuracy	feed imbalance and batch variability
UPM-009	Bioreactor foam probe / antifoam control	foam sensing and antifoam limits	overflow, contamination or filter fouling
UPM-010	Bioreactor headspace pressure	sterile gas and relief devices	vessel breach or backflow
UPM-011	Off-gas oxygen and carbon dioxide analysis	analyzer calibration and sample integrity	misleading metabolism control
UPM-012	Online Raman/NIR process monitoring	model calibration and prediction accuracy	wrong automated process adjustments
UPM-013	Fed-batch nutrient feed pumps	glucose and amino acid feed accuracy	lactate/ammonia rise and quality shift
UPM-014	Perfusion cell retention device	ATF/TFF filter integrity and shear	cell leakage or process failure
UPM-015	Perfusion bleed rate	viable cell density control	instability in growth/quality
UPM-016	Culture osmolality	salt and metabolite accumulation	glycosylation or aggregation drift
UPM-017	Culture metabolite sampling	glucose, lactate, glutamine, ammonia	control decisions based on poor results
UPM-018	In-process cell count analyzer	viability, counting and sample prep	late harvest or inadequate control
UPM-019	Bioreactor disposable probes	installation and calibration checks	unnoticed CPP deviation
UPM-020	Bioreactor electronic batch recipe	validated setpoints and recipe version	wrong process stage executed
UPM-021	Bioreactor harvest trigger	cell viability/impurity threshold	proteolysis and product degradation
UPM-022	Bioreactor gas supply quality	sterile filtration and gas specification	culture contamination / gas impurities
UPM-023	Cell culture contamination detection	bacteria, fungi, mycoplasma and adventitious virus	unsafe or failed product batch
UPM-024	Bioreactor emergency power	control continuity during outages	entire batch loss and uncontrolled culture
UPM-025	Scale-up mixing comparability	shear, kLa, CO2 and temperature gradients	unanticipated CQA change
UPM-026	Media/feed lot change	trace-metal and raw material variability	batch-to-batch product variability

35 | VACCINE / ANTIGEN MANUFACTURING

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
VAC-001	Seed strain authenticity	identity, passage and virulence markers	wrong vaccine strain
VAC-002	Live attenuated seed stability	reversion risk and genetic markers	loss of attenuation
VAC-003	Cell substrate infection multiplicity	MOI, propagation and harvest	inconsistent antigen content
VAC-004	Embryonated egg inoculation	egg source, isolation and contamination	adventitious agents in vaccine bulk
VAC-005	Live vaccine propagation containment	pressure and aerosol controls	live biological release / contamination
VAC-006	Virus harvest pooling	infectivity and antigen identity	incorrect pool potency
VAC-007	Viral inactivation kinetics	inactivant concentration and time	residual infectious agent
VAC-008	Inactivation chemical residuals	formaldehyde/BEI residue specification	toxicity in final vaccine
VAC-009	Inactivation completion testing	sensitivity and representative batches	live virus remains in product
VAC-010	Antigen purification chromatography	host-cell impurities and specificity	unacceptable reactogenicity
VAC-011	Antigen adsorption to adjuvant	bound fraction and kinetics	inconsistent immunogenicity
VAC-012	Aluminium adjuvant preparation	particle size, pH and content	altered adjuvant safety/potency
VAC-013	Emulsion adjuvant homogeneity	droplet size and distribution	poor immune response or reactogenicity
VAC-014	Combination vaccine antigen compatibility	interactions and antigen ratios	loss of component potency
VAC-015	Preservative concentration and efficacy	antimicrobial activity and toxicity	microbial growth or adverse event
VAC-016	Vaccine multi-dose vial control	preservative/open-vial stability	infection or potency loss after opening
VAC-017	Vaccine potency assay qualification	relative units and biologic variability	weak vaccine batches released
VAC-018	Vaccine cold chain storage	temperature/freeze sensitivity and alarms	loss of immunogenic activity
VAC-019	Virus vaccine biosafety containment	risk group and downstream decon	worker infection or agent release
VAC-020	Vaccines lot release / authority samples	country requirements and traceability	noncompliant lot released

36 | VALIDATION, QUALIFICATION & PPQ

28 distinct assessment topics • 84 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
VAL-001	Validation master plan	scope, product lifecycle and accountability	critical system lacks qualification
VAL-002	URS design qualification	function, CQA and GMP requirements	equipment unfit for intended use
VAL-003	Factory acceptance test	interfaces and control logic	critical functional failure at site
VAL-004	Site acceptance test	installation and integration checks	unrecognized site configuration issue
VAL-005	Equipment installation qualification IQ	drawings, materials and utilities	wrong component used in process
VAL-006	Equipment operational qualification OQ	range, alarm and challenge limits	equipment fails at worst case
VAL-007	Performance qualification PQ	load/product and routine conditions	system not proven in use
VAL-008	Bioreactor process performance qualification	multiple batches/CPP/CQA consistency	unproven commercial control strategy
VAL-009	Fermentation process validation	growth, induction, impurity reproducibility	unreliable microbial product manufacture
VAL-010	Chromatography purification PPQ	resin lifetime and impurity clearance	failure to meet purity routinely
VAL-011	TFF concentration process validation	membrane lifetime and yields	uncontrolled concentration / impurity
VAL-012	Low pH viral inactivation validation	worst-case mixing/time/temperature	uncontrolled viral infectivity risk
VAL-013	Virus filter clearance validation	matrix and throughput worst case	invalid virus reduction assertion
VAL-014	Sterilizing filter process validation	retention, integrity and compatibility	false sterile processing claim
VAL-015	CIP cleaning validation	soil, recovery and hold time	cross-product contamination
VAL-016	SIP sterilization validation	temperature penetration and F0	nonsterile equipment surfaces
VAL-017	Autoclave sterilization PQ	load configuration and biological indicators	nonsterile equipment reaches process
VAL-018	Depyrogenation tunnel validation	endotoxin reduction and heat penetration	pyrogenic container not rejected
VAL-019	Aseptic process simulation program	interventions/shifts/line duration	aseptic process unchallenged
VAL-020	CCIT validation	method sensitivity and product effect	leaky containers released
VAL-021	Lyophilizer cycle PPQ	worst-case vials and residual moisture	unstable lyophilised product
VAL-022	Media and buffer hold-time validation	storage temperatures and bioburden	solution microbial proliferation
VAL-023	DS/DP bulk hold-time study	bioburden, potency and CQA drift	unstable bulk used for batch
VAL-024	Equipment clean and dirty hold	sanitization/recontamination interval	persistent bioburden before use
VAL-025	Process transfer comparability	source/target site CPP and CQA	quality impact of tech transfer missed
VAL-026	Continued process verification CPV	trend, alarms and periodic reassessment	late process drift unnoticed
VAL-027	Transport validation	temperature, shock and packaging	shipping-induced quality failure
VAL-028	Electronic batch record recipe validation	interlocks, calculations and audit trail	systematic manufacturing error

37 | VIAL, SYRINGE & CARTRIDGE FILLING

23 distinct assessment topics • 69 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
FILL-001	Vial washer cycle	wash quality and particle removal	visible contaminants in product
FILL-002	Depyrogenation tunnel	heat distribution and endotoxin reduction	pyrogenic vials enter filling
FILL-003	Vial stopper washing	particulate, detergent and endotoxin	product contamination from stopper
FILL-004	Stopper steam sterilization	F0, load pattern and drying	nonsterile stopper contact
FILL-005	Filling needle position	tip height and splash/foaming	incorrect dose or microbial aerosol
FILL-006	Peristaltic pump filling	tubing fatigue and speed calibration	fill-volume variation and particles
FILL-007	Rotary piston filling	clearance, cleaning and volumetric accuracy	incorrect fill and cross-contamination
FILL-008	Time-pressure filling	pressure and temperature compensation	dose inaccuracy
FILL-009	Filling line in-process weight checks	statistical frequency and acceptance	wrong volume lot release
FILL-010	Vial stoppering depth	partially seated stoppers and force	leaky product container
FILL-011	Crimp seal / capping tool	force and metal cap alignment	container closure failure
FILL-012	Pre-filled syringe plunger insertion	plunger position and vacuum	leakage or trapped gas
FILL-013	Syringe siliconization	silicone load and droplet control	protein particles or device friction
FILL-014	Cartridge fill/closure	piston and crimp seating	leakage and dose failure
FILL-015	Glass vial breakage response	glass containment and line reconciliation	foreign particles or mix-up
FILL-016	Aseptic filler interventions	intervention duration and critical zone	microbial contamination introduced
FILL-017	Filling line stoppage/hold time	approved exposure times	uncontrolled sterile product exposure
FILL-018	Container closure integrity test	helium/dye/HVLD suitability	sterile barrier defects missed
FILL-019	Ampoule tip sealing	flame/laser sealing and thermal damage	leaks or degraded product
FILL-020	Sterile final filtration to filling route	closed path and PUPSIT strategy	microbial risk transferred to fill
FILL-021	Filling line format changeover	line clearance, recipe and parts	wrong presentation or dose
FILL-022	Filling machine calibration and speed	validated speed/fill accuracy	process outside validated state
FILL-023	Visual inspection of filled containers	defect library and reject performance	particles or closure defects accepted

38 | VIRAL VECTOR AND GENE THERAPY

25 distinct assessment topics • 75 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
VECTOR-001	Vector plasmid identity	helper, packaging and transgene sequence	wrong genetic payload
VECTOR-002	AAV vector capsid selection	tropism, serotype and immunogenicity	wrong tissue delivery
VECTOR-003	AAV transfection reagent ratio	plasmid/reagent stoichiometry	low or inconsistent particle yield
VECTOR-004	AAV capsid production cell culture	cell health, yield and purity	poor vector titer and impurity load
VECTOR-005	Full versus empty AAV capsid separation	density and assay resolution	suboptimal potency/increased dose load
VECTOR-006	AAV genome packaging fidelity	ITR and vector genome integrity	unexpected transgene expression
VECTOR-007	AAV residual host cell DNA	purification clearance and assay	potential genomic/immune risk
VECTOR-008	Vector residual helper virus	infectious virus test sensitivity	unintended infection exposure
VECTOR-009	AAV vector aggregation	buffer, shear and freeze exposure	potency loss and immune response
VECTOR-010	Lentiviral producer cell line	integration stability and host cell characterization	uncontrolled viral impurity
VECTOR-011	Lentiviral vector harvest timing	infectious titer and time at temperature	loss of transduction potency
VECTOR-012	Lentiviral envelope protein quality	pseudotype integrity and function	altered vector infectivity
VECTOR-013	Replication competent lentivirus testing	assay design and representative samples	infectious replication-competent agent
VECTOR-014	Replication competent retrovirus testing	assay validation and exposure risk	patient infection hazard
VECTOR-015	Lentiviral vector filtration	filter compatibility and viral titer recovery	inadequate dose or contamination
VECTOR-016	Lentiviral vector cryopreservation	stability at low temperature	loss of infectivity
VECTOR-017	Adenoviral vector propagation	replication and release controls	cross contamination / infectious agent
VECTOR-018	Vector concentration by TFF	shear, membrane and recovery	damaged vector / low activity
VECTOR-019	Vector genomic titer assay	qPCR/ddPCR recovery and reference	wrong dose strength
VECTOR-020	Vector functional titer assay	cell assay and inter-run variability	inaccurate biological dose
VECTOR-021	Vector biodistribution assessment	off-target tissue and persistence	unanticipated toxicity
VECTOR-022	Insertional mutagenesis risk analysis	integration-site monitoring	late oncogenic risk
VECTOR-023	Vector production biosafety containment	BSL and aerosol engineering controls	occupational infection or release
VECTOR-024	Vector clearance from shared facility	validated cleaning/decon and campaign segregation	cross-platform viral carryover
VECTOR-025	Vector raw material traceability	plasmid, cell bank and culture reagents	incomplete root-cause traceback

39 | WAREHOUSE / MATERIALS / COLD CHAIN

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
WH-001	Incoming raw material receipt	identity, damage and temperature	degraded inputs accepted
WH-002	Warehouse material status segregation	quarantine/released/rejected labels	unapproved material issued
WH-003	Biologic DS frozen storage	freezer range and excursion alarms	frozen bulk product degradation
WH-004	Drug product refrigerated storage	2-8 C mapping and monitoring	potency loss during storage
WH-005	Ultra-low freezer -80 C	alarm, backup power and probe location	critical cell stock thaw
WH-006	Liquid nitrogen cell bank storage	level monitoring and access	bank loss or vial identity mix-up
WH-007	Cryogenic tank dry shipper	charge duration and shipper qualification	cell therapy loses viability
WH-008	Shipment lane temperature qualification	seasonal excursions and worst case	unqualified cold chain
WH-009	Thermal packaging material qualification	PCM conditioning and pack-out	thermal protection fails in transit
WH-010	Cold room temperature mapping	door opening and load patterns	unrecognized hot or cold spots
WH-011	Distribution data logger calibration	measurement uncertainty and probe placement	false acceptable shipment data
WH-012	Transport excursion investigation	exposure, stability and disposition	compromised product released
WH-013	Controlled substance/restricted biologics	security and traceability obligations	unauthorized diversion or loss
WH-014	Warehouse FEFO system	expiry/hold and inventory transactions	expired biologic dispatched
WH-015	Material dispensing line clearance	identity and tote cleaning	wrong component in process
WH-016	Warehouse pest control	biological contamination and trap records	adventitious material exposure
WH-017	Hazardous microorganism shipment	GMO classification and packaging compliance	infectious material release in transit
WH-018	Clinical site shipment verification	patient ID, site and delivery window	wrong-patient therapy supplied
WH-019	Returned biologic disposition	temperature history and tamper evidence	returned compromised batch reused
WH-020	Warehouse emergency plan	power, freezer spare capacity and drills	irreversible biologic stock loss

40 | WATER, STEAM, GASES & UTILITIES

21 distinct assessment topics • 63 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
WAT-001	Purified-water generation RO	conductivity, flow and membrane integrity	ionic/microbial contamination
WAT-002	WFI generation distillation / membrane	microbial/endotoxin and design controls	pyrogenic process water
WAT-003	WFI storage and distribution loop	temperature, flow and biofilm	endotoxin/bioburden introduced
WAT-004	Water loop sanitization	hot/ozone/chemical exposure and efficacy	persistent microorganisms
WAT-005	Water loop deadlegs and use-point design	slope, velocity and drainability	biofilm and endotoxin reservoir
WAT-006	Purified water sampling plan	worst-case points and frequency	microbial trend missed
WAT-007	WFI endotoxin method	sample recovery and limits	pyrogenic water accepted
WAT-008	WFI TOC/ conductivity monitoring	instrument calibration and alarm limits	ionic/organic breakthrough missed
WAT-009	Clean steam generator feedwater	quality and noncondensable gases	sterilization process inadequacy
WAT-010	Clean steam point of use	steam dryness and superheat	poor heat transfer for sterilization
WAT-011	Compressed process air system	oil, particulate, microbes, dew point	direct product contamination
WAT-012	Compressed nitrogen system	gas identity, oxygen and microbial quality	oxidation or contamination
WAT-013	Process oxygen supply	identity, purity and particulate grade	cell culture quality variability
WAT-014	CO2 supply for cell culture	purity, moisture and gas mixing	culture pH drift
WAT-015	0.22 micron process gas filter	integrity and service lifetime	contaminated gas enters sterile vessel
WAT-016	Utility failure alarm setpoints	critical CPP interface and alarm escalation	process silently outside control
WAT-017	Backflow protection for critical gases	check valves and pressure balance	cross-contaminated gas manifold
WAT-018	Cooling water utility	temperature and leak protection	uncontrolled bioreactor heat removal
WAT-019	Chilled glycol solution	temperature and leak cross-connection	toxic cooling fluid contaminates product
WAT-020	Plant electrical harmonics and grounding	critical instruments and UPS	unreliable control signals
WAT-021	Biological effluent drain decon	inactivation efficiency and discharge limits	live biological release

41 | MRNA / LNP PLATFORMS

20 distinct assessment topics • 60 associated risk scenarios in the Excel register

Review each applicable activity at actual equipment/product level, with documented impact and approved controls. Where not applicable, retain a justified exclusion.

Topic ID	Equipment / process / activity	Critical parameter / failure control	Potential quality / safety consequence
MRNA-001	DNA template sequence confirmation	sequence and plasmid backbone purity	incorrect RNA drug substance
MRNA-002	Linearization of DNA template	complete cut and nucleases	truncated or heterogeneous RNA
MRNA-003	In-vitro transcription reaction	enzyme, NTP and temperature controls	incomplete/impure mRNA
MRNA-004	RNA cap formation efficiency	cap structure and percentage	reduced translation/potency
MRNA-005	Poly(A) tail characterization	length distribution and control	RNA stability/translation drift
MRNA-006	Double stranded RNA impurity	dsRNA assay and removal efficiency	inflammatory response risk
MRNA-007	Residual DNA template clearance	DNase and purification performance	residual DNA in drug product
MRNA-008	Residual nucleotide/enzyme clearance	process purification and assay	unexpected toxicity/instability
MRNA-009	mRNA integrity / fragment profile	RNA electrophoresis and fragment criteria	reduced expression and potency
MRNA-010	RNase-free processing environment	operator and material controls	rapid mRNA degradation
MRNA-011	Lipid identity and ratio	ionizable lipid, cholesterol, phospholipid, PEG	unstable or unsafe LNP
MRNA-012	Microfluidic LNP mixing	flow-rate ratio and total flow rate	wrong particle size/encapsulation
MRNA-013	LNP particle size/PDI	DLS method and acceptance	altered biodistribution or potency
MRNA-014	mRNA encapsulation efficiency	free RNA assay and sampling	variable delivered dose
MRNA-015	LNP residual ethanol clearance	solvent levels and UF/DF controls	patient solvent exposure
MRNA-016	PEG-lipid stability and shedding	composition, temperature and storage	particle instability
MRNA-017	LNP sterile filtration feasibility	pore/filter compatibility and particle recovery	inadequate sterility assurance
MRNA-018	LNP freeze-thaw profile	cryoprotectant and number of cycles	particle rupture or aggregation
MRNA-019	mRNA-LNP potency / expression assay	cell assay validity and reference standards	ineffective lot released
MRNA-020	LNP lipid oxidation/hydrolysis	peroxide and stability-indicating methods	reactogenic or ineffective product

GLOBAL GMP, BIOLOGICS & TURNKEY CONSULTANCY

INDIA + IRELAND / EUROPE

ISHA'S GMP CONSULTANCY PRIVATE LIMITED | INDIA

Chennai office: Regency Flat, Sri Hi-Tech Construction, 55/66, 1st Cross Street, CRR Puram, L&T Colony, Manapakkam, Chennai - 600125, Tamil Nadu, India

Telephone: +91 86675 89984 | +91 99764 91578

Email: info@ishasgmp.com | project@ishasgmp.com

Website: www.ishasgmp.com

Regional office: 338, 3rd Floor, Shoppers Gate, Vapi-Chala Road, Vapi, Gujarat - 396191

ISHA'S GMP TURNKEY CONSULTANCY EUROPE LIMITED | IRELAND

Ireland office: 3 Graydon Green, Newcastle, Dublin, D22 Y9V9, Ireland

Telephone: +353 89 989 1842

Email: info@ishasgmpeu.ie

Website: www.ishasgmpeu.ie

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